

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**

What we claim is:

1) A method for the prophylactic or therapeutic treatment of *Streptococcus pneumoniae*, comprising:

5 administering to the site of an infection or colonization an effective amount of at least one lytic enzyme genetically coded for by a bacteriophage specific for *Streptococcus pneumoniae*, wherein said at least one said lytic enzyme is specific for and has the ability to digest a cell wall of said bacteria, said at least one said lytic enzyme being selected from the group consisting of lytic enzymes, shuffled lytic enzymes, chimeric lytic enzymes, and
10 combinations thereof.

2) The method according to claim 1, wherein said at least one lytic enzyme is produced by recombinant production from a nucleic acid that comprises a DNA having the sequence of bases 3687 to 4577 of SEQ ID No. 2 or a sequence that hybridizes with the complement
15 of bases 3687 to 4577 of SEQ ID No. 2 under stringent hybridization conditions.

3) The method according to claim 1, further comprising delivering said lytic enzyme in a carrier suitable for delivering said lytic enzyme to the site of the infection.

20 4) The method according to claim 3, wherein said carrier is selected from the group consisting of nasal sprays, nasal drops, nasal inhalants, nasal ointments, nasal washes, nasal injections, nasal drops, nasal ointments, nasal washes, nasal injections, gels, nasal packings, ointments, lozenges, troches, candies, injectants, chewing gums, tablets, powders, sprays, injectants, powders, and liquids.

25 5) The method according to claim 4, further comprising delivering a dry anhydrous version of the enzyme by an inhaler.

6) The method according to claim 1, further comprising delivering said lytic enzyme
30 parenterally.

7) The method according to claim 7, wherein said lytic enzyme is delivered intravenously.

8) The method according to claim 7, wherein said lytic enzyme is delivered intramuscularly.

9) The method according to claim 7, wherein said lytic enzyme is delivered subdermally.

10) The method according to claim 7, wherein said lytic enzyme is delivered intrathecally.

11) The method according to claim 1, wherein said bacteriophage is selected from the group consisting of Dp-1, Dp-4, Cp-1, Cp-7, Cp-9, Cp-5, MM1, EJ-1, HB-3, HB-623, HB-746, ω -1, and ω -2.

12) The method according to claim 11, wherein said bacteriophage is Dp-1.

13) A method for treating an upper respiratory tract illness or colonization caused by *Streptococcus pneumoniae*, comprising administering to a mouth, throat, or nasal passage of a mammal a composition comprising:

an effective amount of at least one lytic enzyme genetically coded for by a bacteriophage specific for *Streptococcus pneumoniae*, wherein said at least one said lytic enzyme is specific for and has the ability to digest a cell wall of said bacteria, said at least one said lytic enzyme being selected from the group consisting of lytic enzymes, shuffled lytic enzymes, chimeric lytic enzymes, and combinations thereof.

14) The method according to claim 14, wherein said composition further comprises a carrier selected from the group consisting of nasal sprays, nasal drops, nasal inhalants, nasal ointments, nasal washes, nasal injections, nasal drops, nasal ointments, nasal washes, nasal injections, gels, nasal packings, ointments, lozenges, troches, candies, injectants, chewing gums, tablets, powders, sprays, injectants, powders, intravenous solution, and liquids.

15) The method according to claim 13, wherein said at least one lytic enzyme is produced by recombinant production from a nucleic acid that comprises a DNA having the sequence of bases 3687 to 4577 of SEQ ID No. 2 or a sequence that hybridizes with the complement of bases 3687 to 4577 of SEQ ID No. 2 under stringent hybridization conditions.

5

16) The method according to claim 13, wherein said bacteriophage is selected from the group consisting of Dp-1, Dp-4, Cp-1, Cp-7, Cp-9, Cp-5, MM1, EJ-1, HB-3, HB-623, HB-746, ω -1, and ω -2.

10 17) The method according to claim 16, wherein said bacteriophage is Dp-1.

18) The method according to claim 13, wherein said composition is administered parenterally.

15 19) A method of treating bacterial meningitis caused by *Streptococcus pneumoniae*, comprising:

administering to the site of an infection or colonization an effective amount of at least one lytic enzyme genetically coded for by a bacteriophage specific for *Streptococcus pneumoniae*, wherein said at least one said lytic enzyme is specific for and has the ability to
20 digest a cell wall of said bacteria, said at least one said lytic enzyme being selected from the group consisting of lytic enzymes, shuffled lytic enzymes, chimeric lytic enzymes, and combinations thereof.

20 20) The method according to claim 19, wherein said composition is administered parenterally.

21) The method according to claim 19, wherein said composition is administered intrathecally.

30 22) The method according to claim 19, wherein said composition further comprises a

carrier.

23) The method according to claim 22, wherein said carrier is selected from the group consisting of distilled water, a saline solution, albumin, a serum, Ringer's solution, a buffered solution, a dextrose solution, and combinations thereof.

24) The method according to claim 19, wherein said at least one lytic enzyme is produced by recombinant production from a nucleic acid that comprises a DNA having the sequence of bases 3687 to 4577 of SEQ ID No. 2 or a sequence that hybridizes with the complement of bases 3687 to 4577 of SEQ ID No. 2 under stringent hybridization conditions.

25) The method according to claim 19, wherein said bacteriophage is selected from the group consisting of Dp-1, Dp-4, Cp-1, Cp-7, Cp-9, Cp-5, MM1, EJ-1, HB-3, HB-623, HB-746, ω -1, and ω -2.

26) The method according to claim 25, wherein said bacteriophage is Dp-1.

27) A method for treating, preventing or ameliorating a *Streptococcus pneumoniae* infection at a mucosal surface, comprising the steps of :

a) administering to the site of an infection or colonization an effective amount of at least one lytic enzyme genetically coded for by a bacteriophage specific for *Streptococcus pneumoniae*, wherein said at least one said lytic enzyme is specific for and has the ability to digest a cell wall of said bacteria, said at least one said lytic enzyme being selected from the group consisting of lytic enzymes, shuffled lytic enzymes, chimeric lytic enzymes, and combinations thereof; and

b) applying said composition to the mucosal surface.

28) The method according to claim 27, wherein said at least one lytic enzyme is produced by recombinant production from a nucleic acid that comprises a DNA having the sequence of bases 3687 to 4577 of SEQ ID No. 2 or a sequence that hybridizes with the complement

of bases 3687 to 4577 of SEQ ID No. 2 under stringent hybridization conditions.

29) The method according to claim 28, wherein said bacteriophage is selected from the group consisting of Dp-1, Dp-4, Cp-1, Cp-7, Cp-9, Cp-5, MM1, EJ-1, HB-3, HB-623, HB-746, -1, and -2.

30) The method according to claim 29, wherein said bacteriophage is Dp-1.

31) A method of treating eyes exposed to *Streptococcus pneumoniae*, comprising:

administering to the eyes an effective amount of at least an effective amount of at least one lytic enzyme genetically coded for by a bacteriophage specific for *Streptococcus pneumoniae*, wherein said at least one said lytic enzyme is specific for and has the ability to digest a cell wall of said bacteria, and wherein a genetic code for said at least one said lytic enzyme is altered, such that said at least one said lytic enzyme is selected from the group consisting of shuffled lytic enzymes, chimeric lytic enzymes, and combinations thereof.

32) The method according to claim 31, wherein said carrier is an eye drop solution.

33) The method according to claim 31, wherein said at least one lytic enzyme is produced by recombinant production from a nucleic acid that comprises a DNA having the sequence of bases 3687 to 4577 of SEQ ID No. 2 or a sequence that hybridizes with the complement of bases 3687 to 4577 of SEQ ID No. 2 under stringent hybridization conditions.

34) The method according to claim 31, wherein said bacteriophage is selected from the group consisting of D-1, DP-4, Cp-1, Cp-7, Cp-9, Cp-5, MM1, EJ-1, HB-3, HB-623, HB-746, ω -1, and ω -2.

35) The method according to claim 34, wherein said bacteriophage is Dp-1.

36) A method for treating ear infections, comprising administering to a canal of an ear an

effective amount of an effective amount of at least one lytic enzyme genetically coded for by a bacteriophage specific for *Streptococcus pneumoniae*, wherein said at least one said lytic enzyme is specific for and has the ability to digest a cell wall of said bacteria, said at least one said lytic enzyme is selected from the group consisting of lytic enzymes, shuffled
5 lytic enzymes, chimeric lytic enzymes, and combinations thereof.

37) The method according to claim 36, wherein said at least one lytic enzyme is produced by recombinant production from a nucleic acid that comprises a DNA having the sequence of bases 3687 to 4577 of SEQ ID No. 2 or a sequence that hybridizes with the complement
10 of bases 3687 to 4577 of SEQ ID No. 2 under stringent hybridization conditions.

38) The method according to claim 36, wherein said bacteriophage is selected from the group consisting of Dp-1, DP-4, Cp-1, Cp-7, Cp-9, Cp-5, MM1, EJ-1, HB-3, HB-623, HB-746, ω -1, and ω -2.

15

39) The method according to claim 38, wherein said bacteriophage is Dp-1.

40) A method for preventing infection of contact lens solution by *Streptococcus pneumoniae*, comprising the steps of:

20 administering to said contact lens solution an effective amount of at least one lytic enzyme genetically coded for by a bacteriophage specific for *Streptococcus pneumoniae*, wherein said at least one said lytic enzyme is specific for and has the ability to digest a cell wall of said bacteria, said at least one said lytic enzyme being selected from the group consisting of shuffled lytic enzymes, chimeric lytic enzymes, and combinations thereof.

25

41) The method according to claim 40, wherein said at least one lytic enzyme is produced by recombinant production from a nucleic acid that comprises a DNA having the sequence of bases 3687 to 4577 of SEQ ID No. 2 or a sequence that hybridizes with the complement of bases 3687 to 4577 of SEQ ID No. 2 under stringent hybridization conditions.

30

42) The method according to claim 40, wherein said bacteriophage is selected from the group consisting of Dp-1, DP-4, Cp-1, Cp-7, Cp-9, Cp-5, MM1, EJ-1, HB-3, HB-623, HB-746, ω -1, and ω -2.

5 43) The method according to claim 42, wherein said bacteriophage is Dp-1.

44) The method according to claim 40, wherein said contact lens solution is an isotonic solution.

10 45) The method according to claim 40, wherein said contact lens solution further comprises sodium chloride, sugar alcohols, borates, preservatives, and combinations thereof.

15 46) A method for treating endocarditis caused by *Streptococcus pneumoniae*, comprising administering to site of the infection an effective amount of an effective amount of at least one lytic enzyme genetically coded for by a bacteriophage specific for *Streptococcus pneumoniae*, wherein said at least one said lytic enzyme is specific for and has the ability to digest a cell wall of said bacteria, said at least one said lytic enzyme is selected from the group consisting of lytic enzymes, shuffled lytic enzymes, chimeric lytic enzymes, and
20 combinations thereof.

47) The method according to claim 46, wherein said at least one lytic enzyme is produced by recombinant production from a nucleic acid that comprises a DNA having the sequence of bases 3687 to 4577 of SEQ ID No. 2 or a sequence that hybridizes with the
25 complement of bases 3687 to 4577 of SEQ ID No. 2 under stringent hybridization conditions.

48) The method according to claim 46, further comprising delivering said lytic enzyme in a carrier suitable for delivering said lytic enzyme to the site of the infection.

49) The method according to claim 46, wherein said bacteriophage is selected from the group consisting of Dp-1, DP-4, Cp-1, Cp-7, Cp-9, Cp-5, MM1, EJ-1, HB-3, HB-623, HB-746, ω -1, and ω -2.

5 50) The method according to claim 49, wherein said bacteriophage is Dp-1.

51) The method according to claim 48, wherein said carrier is selected from the group consisting of distilled water, a saline solution, albumin, a serum, fixed oils, liposomes, ethyl oleate, and combinations thereof.

10

52) The method according to claim 51, wherein said carrier may further comprise preservatives, stabilizers, buffers, gelatin, a vasoconstriction agent, amino acids, antioxidants, polypeptides, hydrophilic polymers, sugar alcohols, chelating agents, sugars, counter ions, non-ionic surfactants, and combinations thereof.

15

53) A method for the treating the carriage of *Streptococcus pneumoniae* in the upper respiratory tract illness, comprising administering to a mouth, throat, or nasal passage of a mammal a composition comprising an effective amount of an effective amount of at least one lytic enzyme genetically coded for by a bacteriophage specific for *Streptococcus pneumoniae*, wherein said at least one said lytic enzyme is specific for and has the ability to digest a cell wall of said bacteria, said at least one said lytic being selected from the group consisting of shuffled lytic enzymes, chimeric lytic enzymes, and combinations thereof.

20

54) The method according to claim 53, wherein said composition further comprises a carrier selected from the group consisting of nasal sprays, nasal drops, nasal inhalants, nasal ointments, nasal washes, nasal injections, nasal ointments, nasal injections, gels, nasal packings, ointments, lozenges, troches, candies, injectants, chewing gums, tablets, powders, sprays, injectants, powders, intravenous solution, and liquids..

25

30 55) The method according claim 53, wherein said at least one lytic enzyme is present in a

concentration of about 100 to about 500,000 active enzyme units per milliliter of fluid in the wet environment of the nasal or oral passages.

56) The method according to claim 53, wherein said composition is administered parenterally.

57) The method according to claim 53, wherein said at least one lytic enzyme is produced by recombinant production from a nucleic acid that comprises a DNA having the sequence of bases 3687 to 4577 of SEQ ID No. 2 or a sequence that hybridizes with the complement of bases 3687 to 4577 of SEQ ID No. 2 under stringent hybridization conditions.

58) A composition for treating *Streptococcus pneumoniae*, comprising:

a) an effective amount of at least one lytic enzyme genetically coded for by a bacteriophage specific for *Streptococcus pneumoniae*, wherein said at least one said lytic enzyme is specific for and has the ability to digest a cell wall of said bacteria, said at least one said lytic enzyme being selected from the group consisting of shuffled lytic enzymes, chimeric lytic enzymes, and combinations thereof; and

b) a carrier.

59) The composition according to claim 58, wherein said at least one lytic enzyme is produced by recombinant production from a nucleic acid that comprises a DNA having the sequence of bases 3687 to 4577 of SEQ ID No. 2 or a sequence that hybridizes with the complement of bases 3687 to 4577 of SEQ ID No. 2 under stringent hybridization conditions.

60) The composition according to claim 58, wherein said carrier is selected from the group consisting of nasal sprays, nasal drops, nasal inhalants, nasal ointments, nasal washes, nasal injections, nasal drops, nasal ointments, nasal washes, nasal injections, gels, nasal packings, lozenges, troches, candies, injectants, chewing gums, tablets, powders, sprays, injectants, powders, and liquids.

61) The composition according to claim 60, further comprising delivering a dry anhydrous version of the enzyme by an inhaler.

62) The composition according to claim 58, wherein said bacteriophage is selected from the group consisting of Dp-1, Dp-4, Cp-1, Cp-7, Cp-9, Cp-5, MM1, EJ-1, HB-3, HB-623, HB-746, ω -1, and ω -1.

63) The composition according to claim 62, wherein said bacteriophage is Dp-1.

64) The composition according to claim 58, further comprising an antibiotic.

65) A composition for treating a respiratory tract illnesses caused by *Streptococcus pneumoniae*, wherein said composition is formed by:

i) obtaining an effective amount of at least one lytic enzyme genetically coded for by a bacteriophage specific for *Streptococcus pneumoniae*, wherein said at least one said lytic enzyme is specific for and has the ability to digest a cell wall of said bacteria, said at least one said lytic enzyme being selected from the group consisting of lytic enzymes, shuffled lytic enzymes, chimeric lytic enzymes, and combinations thereof; and

ii) incorporating said lytic enzyme into a carrier which can deliver said lytic enzyme to said mouth, throat, or nasal passage of a mammal.

66) The composition according to claim 65, wherein said carrier is suitable for delivering said lytic enzyme parenterally.

67) The composition according to claim 65, wherein said at least one lytic enzyme is produced by recombinant production from a nucleic acid that comprises a DNA having the sequence of bases 3687 to 4577 of SEQ ID No. 2 or a sequence that hybridizes with the complement of bases 3687 to 4577 of SEQ ID No. 2 under stringent hybridization conditions.

68) A parenteral solution for treating bacterial meningitis caused by *Streptococcus pneumoniae*, wherein said composition is formed by the method comprising the steps of:

i) obtaining an effective amount of at least one lytic enzyme genetically coded for by a bacteriophage specific for *Streptococcus pneumoniae*, wherein said at least one said lytic enzyme is specific for and has the ability to digest a cell wall of said bacteria, and wherein a genetic code for said at least one said lytic enzyme is altered, such that said at least one said lytic enzyme is selected from the group consisting of shuffled lytic enzymes, chimeric lytic enzymes, and combinations thereof.; and

ii) incorporating said at least one said lytic enzyme into a carrier deliver said lytic enzyme parenterally.

69) The composition according to claim 210, wherein said at least one

lytic enzyme is produced by recombinant production from a nucleic acid that comprises a DNA having the sequence of bases 3687 to 4577 of SEQ ID No. 2 or a sequence that hybridizes with the complement of bases 3687 to 4577 of SEQ ID No. 2 under stringent hybridization conditions.

70) The composition according to claim 68, wherein said carrier is selected from the group consisting of distilled water, a saline solution, albumin, a serum, Ringer's solution, a buffered solution, a dextrose solution, and combinations thereof.

71) The composition according to claim 68, wherein said carrier comprises additives selected from the group consisting of p-hydroxybenzoates, stabilizers, fixed oils, ethyl oleate, neutral salts, dextrose, trehalose, dextrans, lactose, phosphate buffered saline, gelatin, albumin, vasoconstriction agents, organic acids organic acid salts, antioxidants, low molecular weight polypeptides, proteins, immunoglobulins, hydrophilic polymers, amino acids, monosaccharides, disaccharides, other carbohydrates including cellulose or its derivatives, glucose, chelating agents, sugar alcohols, counter-ions, non-ionic surfactants, glycerin, glycerol, DMSO, and combinations thereof.

72) An eye drop solution for treating eyes exposed to *Streptococcus pneumoniae* wherein said composition is formed by the method comprising the steps of:

a) obtaining an effective amount of at least one lytic enzyme genetically coded for by a bacteriophage specific for *Streptococcus pneumoniae*, wherein said at least one said lytic enzyme is specific for and has the ability to digest a cell wall of said bacteria, and wherein
5 a genetic code for said at least one said lytic enzyme is altered, such that said at least one said lytic enzyme is selected from the group consisting of shuffled lytic enzymes, chimeric lytic enzymes, and combinations thereof, and

b) incorporating said lytic enzyme into an isotonic solution serving as a carrier
10 which can deliver said lytic enzyme to said eyes.

73) The composition according to claim 72, wherein said at least one lytic enzyme is produced by recombinant production from a nucleic acid that comprises a DNA having the sequence of bases 3687 to 4577 of SEQ ID No. 2 or a sequence that hybridizes with the
15 complement of bases 3687 to 4577 of SEQ ID No. 2 under stringent hybridization conditions.

74) The composition according to claim 72, wherein said bacteriophage is selected from the group consisting of Dp-1, DP-4, Cp-1, Cp-7, Cp-9, Cp-5, MM1, EJ-1, HB-3, HB-623,
20 HB-746, ω -1, and ω -2.

75) The composition according to claim 72, wherein said bacteriophage is Dp-1.

76) A contact lens solution by *Streptococcus pneumoniae*, wherein solution is formed by
25 the steps of:

a) obtaining an effective amount of at least one lytic enzyme genetically coded for by a bacteriophage specific for *Streptococcus pneumoniae*, wherein said at least one said lytic enzyme is specific for and has the ability to digest a cell wall of said bacteria, and wherein
a genetic code for said at least one said lytic enzyme is altered, such that said at least one
30 said lytic enzyme is selected from the group consisting of shuffled lytic enzymes, chimeric

lytic enzymes, and combinations thereof; and

b) incorporating said at least one lytic enzyme into a solution used for cleaning contact lenses.

5 77) The contact lens solution according to claim 76, wherein said at least one lytic enzyme is produced by recombinant production from a nucleic acid that comprises a DNA having the sequence of bases 3687 to 4577 of SEQ ID No. 2 or a sequence that hybridizes with the complement of bases 3687 to 4577 of SEQ ID No. 2 under stringent hybridization conditions.

10

78) The contact lens solution according to claim 76, wherein said bacteriophage is selected from the group consisting of Dp-1, DP-4, Cp-1, Cp-7, Cp-9, Cp-5, MM1, EJ-1, HB-3, HB-623, HB-746, ω -1, and ω -2.

15 79) The contact lens solution according to claim 76, wherein said bacteriophage is Dp-1.

80) The contact lens solution according to claim 76, wherein said contact lens solution is an isotonic solution.

20